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Depressive symptoms predict smoking cessation in a 20-year longitudinal study of adult twins

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HIGHLIGHTS

- Baseline depressive symptoms are associated with lower odds of smoking cessation.
- This association is confounded by baseline heaviness of smoking and familial factors.
- Factors underlying the association of smoking with depression warrant more research.

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ABSTRACT

Depression has been suggested to hinder smoking cessation, especially when co-occurring with nicotine dependence. The study aimed to examine the longitudinal association of depressive symptoms with smoking cessation among daily smokers. The study utilized adult Finnish twin cohort where 1438 daily smokers (mean age: 38.3, range: 33–45) in 1990 were re-examined for their smoking status in 2011. We assessed baseline depressive symptoms with the Beck Depression Inventory, and the self-reported smoking status at follow-up. The methods included multinomial logistic regression and time to event analyses, adjusted for multiple covariates (age, sex, marital status, social class, heavy drinking occasions, and health status) and smoking heaviness at baseline assessed by cigarettes per day (CPD). Additionally, within-twin-pair analyses were conducted. Results indicated that moderate/severe depressive symptoms at baseline were associated with a lower likelihood of smoking cessation two decades later. Adjusting for covariates, those with moderate/severe depressive symptoms (vs. no/minimal depressive symptoms) had 46% lower likelihood of quitting (relative risk ratio, RRR = 0.54, 95% CI: 0.30–0.96). After including CPD, the association of depressive symptoms with smoking cessation attenuated modestly (RRR = 0.62, 95% CI: 0.34–1.12). Further, time to event analysis for quitting year since baseline yielded similar findings. In the within-pair analysis, depressive symptoms were not associated with quitting smoking. The results suggest that reporting more depressive symptoms is associated with a lower likelihood of smoking cessation during a 20-year period. The baseline amount of smoking and familial factors partly explain the observed association. Smoking cessation programs should monitor depressive symptoms.

1. Introduction

Tobacco use is a major cause of mortality and morbidity, especially among individuals with a psychiatric disorder (Royal College of Psychiatrists, 2013). Quitting smoking reduces smoking-related mortality (Thun et al., 2013). However, quitting may be especially challenging for depressed smokers (Ruther et al., 2014). Smokers with psychiatric comorbidity may be as motivated to quit (Siru, Hulse, & Tait, 2009), but more likely to relapse compared to general population (Weinberger et al., 2017). To better understand the relationship between depressive symptoms and smoking cessation, it is crucial to investigate the association and its underlying mechanisms with long-term prospective data.

Several factors influence smoking behavior and cessation. Smokers easily become nicotine dependent as nicotine facilitates the release of various neurotransmitters, for example, serotonin and dopamine (Bruijnzeel, 2012; Picciotto, Brunzell, & Caldarone, 2002), while chronic and high intake of nicotine results in adaptation in nicotinic

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pathways of the brain (Balfour & Ridley, 2000). Smokers with a comorbid depressive disorder may continue smoking to relieve their symptoms, as suggested by the self-medication hypothesis (Khantzian, 2003). This is because nicotine may provide short-term compensation for existing deficits in the cholinergic system, for example, related to cognition, attention, arousal, motivational behaviors, and food satiety (Laje, Berman, & Glassman, 2001). However, challenging this scenario, smoking has been associated with an increase of depressive symptoms (Vermeulen et al., 2019; Wootton et al., 2019), and smoking cessation with improved mental health, wellbeing, and quality of life (Taylor et al., 2014).

Furthermore, low positive or high negative affect, cognitive impairment, inability to feel pleasure, anxiety sensitivity, and distress tolerance have been found to be associated with relapse and unsuccessful quitting (Ameringer & Leventhal, 2010; Leventhal & Zvolensky, 2015; Mathew, Hogarth, Leventhal, Cook, & Hitsman, 2017). Thus, compared to non-depressed smokers, depressed smokers exhibit a higher negative affective state, which may promote continued smoking behavior.

Additionally, the association between depression and smoking cessation could be attributable to shared familial factors (Rose, Broms, Korhonen, Dick, & Kaprio, 2009). Smoking behavior is genetically correlated with major depressive disorder (Liu et al., 2019). However, despite the underlying mechanisms, successful quitting predicts a decrease in depressive symptoms (Taylor et al., 2014), whereas, unsuccessful quitters are more likely to experience depression later (McClave et al., 2009). Moreover, patients with depression can successfully quit smoking if provided with effective interventions (Gierisch, Bastian, Calhoun, McDuffie, & Williams, 2012; Secades-Villa, Gonzalez-Roz, Garcia-Perez, & Becona, 2017).

Longitudinal population-based studies are important as they provide information on the nature of the association in an unselected population of smokers. In this study, we seek to describe and better understand the association between depressive symptoms and smoking cessation outcome after 20 years of follow-up in adulthood. The main aim of the present study was to investigate whether depressive symptoms predict poor smoking cessation outcome. If so, our further research question was whether the observed association is independent of confounding factors.

2. Method

2.1. Sample

The Adult Finnish Twin Cohort is a population-based sample compiled from the Central Population Registry consisting of all same sex twin pairs born in Finland before 1958 with surveys starting in 1975. Next surveys of the cohort were in 1981, 1990, and 2011, respectively (Kaprio & Koskenvuo, 2002; Kaprio et al., 2019). This specific study utilized data from the third and fourth waves of the surveys. In 1990, a questionnaire was sent to twins born in 1930–1957, who had responded to one of the previous surveys. The response rate was 77%, with 12,502 respondents. In 2011, a questionnaire was sent to twins born 1945–1957 irrespective of participation in any earlier survey. Out of 11,766 persons alive and residing in Finland, 8410 responded, yielding a response rate of 72%. In the 1990 survey, 3053 participants reported being a current daily smoker and responded to items on depressive symptoms. Of daily smokers in the 1990 survey, 1473 participated in the 2011 questionnaire survey (1189 born in 1930–1944 or died were excluded and 391 did not participate the follow-up). After including only those who had provided complete information on smoking status at the 2011 follow-up and depressive symptoms in 1990, we studied 1438 participants. The mean age at the baseline was 38.3 years. There were 693 males and 745 females. Of the participants, 459 (31.9%) were monozygotic (MZ) twins, 881 (61.3%) were dizygotic (DZ) twins, and 98 (6.8%) were of unknown zygosity. Ethical permissions for the Adult Twin Cohort surveys were obtained from the Ethics committee of the Department of Public Health, University of Helsinki and University District Hospital of Helsinki and Uusimaa, Finland.

2.2. Measures

2.2.1. Depressive symptoms

The 1990 baseline survey assessed depressive symptoms using the Beck Depression Inventory (BDI), the 21-item questionnaire where instructions guide the participants in describing their symptoms and attitudes as they perceive them 'right now' in terms of intensity from 0 to 3 (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). The BDI has high internal consistency, with alpha coefficient of 0.86 for depressed and 0.81 for non-depressed population (Beck, Steer, & Carbin, 1988). The BDI sum score ranges from 0 to 63. We created three depression categories based on the sum scores: 1) 0–9 (none or minimal depression); 2) 10–16 (mild depression); and 3) 17 or higher (moderate/severe depression) which is nearly identical to the guidelines for BDI cut-points of scores (Beck et al., 1988). More details of BDI have been provided in a previous study based on the 1990 survey (Varjonen, Romanov, Kaprio, Heikkilä, & Koskenvuo, 1997). For the analysis, the BDI sum score was also utilized as a continuous variable (min–max score: 0–37). In sensitivity analyses, we used the Center for Epidemiologic Studies Depression (CES-D) scale to assess depressive symptoms at the follow-up (Radloff, 1977). The CES-D scale includes 20 items assessing frequency of depressive symptoms and ranging from 0 to 3. The sum score ranged from 0 to 60, and a cut off value $\geq$ 20 was used to identify a participant with depression (Vilagut, Forero, Barbaglia, & Alonso, 2016).

2.2.2. Smoking status and quitting smoking

To classify smoking status participants were asked, "Have you smoked more than 5–10 packs of cigarettes in your lifetime?", being comparable with the commonly used threshold of 100 cigarettes lifetime exposure. Those responding negatively were considered as *'never smokers'* and those responding positively were further asked, "Do you smoke, or have you smoked cigarettes regularly, say daily or almost daily during your lifetime?" Those who replied negatively were considered as *'occasional smokers';* (i.e. non-daily smokers). Those who replied positively were further queried, "Do you still smoke cigarettes regularly?" If so, they were classified as '*current daily smokers'* and if not, they were classified as '*former smokers'* (regular smokers who had responded that they no longer smoked at the time of the survey) (Kaprio & Koskenvuo, 1988). The present study includes only those who were classified as '*current daily smokers'* at the baseline in 1990. In their subsequent follow-up (2011), smoking status was classified in three categories: 1) Current daily smokers; 2) Occasional smokers; and 3) Former smokers, i.e. successful quitters.

'A time of quitting' since baseline variable was created for time-to-event analysis (see below). In the 2011 questionnaire, respondents were asked, "How old were you when you stopped smoking?". Based on their response and the age at the time of surveys, we created the 'year of quitting' variable. Those who had quit during 1990–2011 were considered as former smokers, and all others (current and occasional smokers in 2011) were censored after the end of follow-up (2011).

2.2.3. Amount of smoking and use of nicotine replacement therapy

Cigarettes smoked per day (CPD) is one of the two items in the Heaviness of Smoking Index (Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989), a short measure of nicotine dependence. To determine CPD at study baseline, participants were asked, "How many cigarettes do you smoke daily on average?" and categorized as "1–9 cigarettes", "10–19 cigarettes", and "20 or more cigarettes".

In sensitivity analyses, we adjusted for use of nicotine replacement therapy (NRT) as a cessation aid. In the 2011 follow-up questionnaire participants were asked "Have you during the past year (12 months)

used nicotine replacement therapy (gum, patch, lozenge etc.)?", the responses classified as "No, I have not used NRT/I have used NRT for other reason than smoking cessation" and "Yes, I have used NRT as a smoking cessation aid". Those who did not use NRT or used NRT for other reason were combined to create a reference category.

2.2.4. Covariates

We included several covariates assessed at baseline, capturing a) sociodemographic factors (age, sex, marital status, and social class); b) health status; and c) heavy drinking occasions (alcohol use). These covariates were considered based on a careful literature review and identified as potential confounders for the association between depression and smoking cessation (Chaiton, Cohen, Rehm, Abdulle, & O'Loughlin, 2015; Huffman, Bromberg, & Augustson, 2018; Weinberger et al., 2017).

For marital status, participants were asked, "What is your marital status?", and the responses were categorized as "married" (including remarried or cohabiting) or "single" (comprising single, divorced and widowed). Social class was defined by years of education and type of work (Appelberg, Romanov, Honkasalo, & Koskenvuo, 1991). Those who had a minimum of 12 years of education and performing sedentary work were categorized "high" ('white collar'); those who had < 9 years of education and performed physical work were "low" ('blue collar') and these remaining represented an intermediate group "medium". To determine health status, a Somatic Disease Index was created based on self-reports. A participant was considered to have a somatic disease if he/she reported one of the following: i) a disease diagnosed by a physician (a list of 20 chronic conditions such as asthma, hypertension, diabetes, and cancer), ii) serious injury/illness or iii) work disability. Others were considered as 'healthy' (Romanov, Varjonen, Kaprio, & Koskenvuo, 2003). To determine heavy drinking occasions (Sipila, Rose, & Kaprio, 2016), participants were asked "Does it happen that at least once a month and on the same occasion you drink more than five bottles of beer or more than a bottle of wine or more than half a bottle of hard liquor?" and the response was categorized as "no" or "yes".

2.3. Statistical analyses

First, we conducted multinomial logistic regression analyses to study the association between baseline depressive symptoms and smoking status at follow-up. BDI was included as a three-category variable (None/Minimal (0–9), Mild (10–16), and Moderate/Severe (17 or more)) based on the sum scores. We also used the BDI sum score as a continuous variable. Daily smokers were used as the reference category of smoking status at follow-up. In the analyses, twins were treated as individuals, but because observations on twins within twin pairs are not independent, cluster-robust standard errors were estimated (Williams, 2000). The analysis was first adjusted for age and sex to estimate the crude association between depressive symptoms and smoking cessation. We then adjusted for marital status, social class, heavy drinking occasions, and health status to observe if the association attenuated after adjusting for multiple confounders. The final model included additionally CPD to test the influence of smoking heaviness on the association. Males and females were pooled together in the analyses because there was no evidence for a sex*depressive symptoms interaction (Likelihood Ratio test, chi2(4) = 4.96, p = 0.29).

To strengthen our findings, we conducted time-to-event analysis to observe if depressive symptoms at baseline predicted timing of quitting smoking. We followed participants from 1990 until 2011 and recorded the year of quitting, therefore, studying the time to event between depressive symptoms and quitting smoking. All analyses were adjusted for the same co-variates. We estimated Relative Risk Ratios (RRR) and Hazard Ratios (HR) with 95% confidence intervals (CI) and considered $p < 0.05$ as statistically significant.

Additionally, we conducted within-pair-analysis as a fixed effects model (conditional logistic regression) (Allison, 2009). In the analysis, to gain statistical power, occasional and daily smokers were pooled as "current smokers" and mild and moderate/severe depressive symptoms into one category. Similarly, MZ and DZ pairs were pooled together. The fixed effects models use data from co-twins who differ regarding depression and thus control for possible unmeasured confounding due to genetic influences and other factors shared by the co-twins.

We conducted two sensitivity analyses. First, we additionally adjusted the analysis with depressive symptoms measured at follow-up. Second, we performed a sensitivity analysis among the sub-sample of remaining smokers vs. quitters during the past year before follow-up. We adjusted the analysis for NRT use during 2010–2011 to observe if the association between depressive symptoms and quitting smoking was explained by pharmacological treatment. All statistical analyses were conducted with Stata (version 15) (StataCorp. , 2015).

3. Results

3.1. Descriptive data

Of daily smokers at baseline, 38% had quit smoking, 6% had become occasional smokers, and more than half remained daily smokers at the follow-up (Table 1). Five percent of participants reported moderate/severe depressive symptoms (mean score: 5.3). Most of those with moderate/severe depressive symptoms, continued to be daily smokers at the follow-up. There were more males than females among quitters. Of those having moderate/severe depressive symptoms, 49% smoked 20 or more CPD whereas the proportion was significantly smaller among those with mild or none/minimal depressive symptoms (Chi2(4) = 18.55, $p < 0.05$; not shown in the Table).

3.2. Association between baseline depressive symptoms and smoking status at follow-up

Having moderate/severe (vs. none/minimal) depressive symptoms halved the likelihood of smoking cessation at follow-up (RRR = 0.50, 95% CI: 0.28–0.89) (Table 2). Adjusting for multiple covariates only slightly attenuated the association (RRR = 0.54, 95% CI: 0.30–0.96). To control for baseline differences in the amount of smoking, CPD was added to the model. The RRR estimate was now more attenuated and statistically non-significant (RRR = 0.62, 95% CI: 0.34–1.12). Further, reporting more depressive symptoms was also associated with a lower likelihood of becoming an occasional smoker, but the association was statistically non-significant (age and sex adjusted RRR = 0.55, 95% CI: 0.17–1.82). When depressive symptoms were analyzed as a continuous variable, the results were consistent with the main analysis (not shown in the Table). Reporting more depressive symptoms predicted a lower likelihood of quitting smoking when adjusted for all covariates except CPD (RRR = 0.98, 95% CI: 0.96–1.00, p = 0.031). Additional adjustment for CPD attenuated the significance but not the point estimate (RRR = 0.98, 95% CI: 0.96–1.01, p = 0.15).

3.3. Association between depressive symptoms and time of quitting

The Cox proportional-hazards models for the time of quitting since baseline provided similar results as the first analysis. Adjusted for age and sex, the Hazard Ratio of smoking cessation among those having moderate/severe (vs. none/minimal) depressive symptoms was 0.58 (95% CI: 0.36–0.96) (Table 3). The association attenuated after adjusting for other covariates. The Kaplan-Meier survival curves show that those reporting higher depressive symptoms were less likely to quit smoking over the follow-up period (Fig. 1).

3.4. Familial factors, depressive symptoms and smoking status: Within-pair analysis

Accounting for shared familial factors in the within-pair analysis, there was no association between depressive symptoms at baseline and

Table 1
Descriptive characteristics of daily smokers in 1990 by smoking status in 2011.

Characteristics	Total	Current daily smokers	Occasional smokers	Former smokers
	N = 1438	N = 799 (55.5%)	N = 90 (6.3%)	N = 549 (38.2%)
BDI (1990)				
None/Minimal (%)	1179 (82.0)	639 (80.0)	75 (83.3)	465 (84.7)
Mild (%)	190 (13.2)	111 (13.9)	12 (13.3)	67 (12.2)
Moderate/Severe (%)	69 (4.8)	49 (6.1)	3 (3.3)	17 (3.1)
BDI score (1990)				
Mean (SD)	5.3 (5.7)	5.8 (6.0)	4.7 (5.1)	4.8 (5.2)
Score min–max	0–37	0–37	0–29	0–34
Median (Q1, Q3)	4 (1,8)	4 (1,8)	3 (1,6)	3 (1,7)
None/Minimal Mean (SD)	3.2 (2.7)	3.4 (2.8)	2.8 (2.5)	3.1 (2.7)
Mild Mean (SD)	12.3 (2.0)	12.4 (2.0)	12.1 (1.9)	12.2 (2.0)
Moderate/Severe Mean (SD)	22.6 (4.8)	22.4 (4.9)	21.3 (6.6)	23.2 (4.6)
Age, Years				
Mean (SD)	38.3 (3.6)	38.1 (3.6)	38.4 (3.5)	38.7 (3.7)
Sex				
Male (%)	693 (48.2)	360 (45.1)	49 (54.4)	284 (51.7)
Female (%)	745 (51.8)	439 (54.9)	41 (45.6)	265 (48.3)
Social class				
Low (%)	676 (47.0)	387 (48.4)	38 (42.2)	251 (45.7)
Medium (%)	644 (44.8)	358 (44.8)	38 (42.2)	248 (45.2)
High (%)	118 (8.2)	54 (6.8)	14 (15.6)	50 (9.1)
Chronic Illness/Disability				
No (%)	682 (47.4)	372 (46.6)	45 (50.0)	265 (48.3)
Yes (%)	756 (52.6)	427 (53.4)	45 (50.0)	284 (51.7)
Marital status				
Married (%)	1061 (73.8)	580 (72.6)	64 (71.1)	417 (76.0)
Single (%)	375 (26.1)	217 (27.2)	26 (28.9)	132 (24.0)
Missing (%)	2 (0.1)	2 (0.2)	0	0
Heavy drinking occasions				
No (%)	732 (50.9)	398 (49.8)	41(45.6)	293 (53.4)
Yes (%)	697 (48.5)	398 (49.8)	48 (53.3)	251 (45.7)
Missing (%)	9 (0.6)	3 (0.4)	1 (1.1)	5 (0.9)
Cigarettes per day				
Up to 9 cigarettes (%)	400 (27.8)	165 (20.7)	51 (56.7)	184 (33.5)
10–19 cigarettes (%)	611 (42.5)	367 (45.9)	19 (21.1)	225 (41.0)
20 or more (%)	421 (29.3)	267 (33.4)	18 (20.0)	136 (24.8)
Missing (%)	6 (0.4)	0	2 (2.2)	4 (0.7)

N = Total number.
SD = Standard Deviation.
Q1 = 1st quartile.
Q3 = 3rd quartile.
BDI = Beck Depression Inventory.

smoking status at follow-up (OR = 1.14, 95% CI: 0.41–3.15, p = 0.80) (Supplementary Table A.1).

3.5. Sensitivity analyses

When adjusting for depressive symptoms at follow-up, the point estimates of the association between baseline depressive symptoms and quitting smoking were very similar to the main results (Supplementary Table A.2). Among the sub-sample of remaining smokers and those who quit during 2010–2011, the association between baseline depressive symptoms and smoking status was not explained by past-year NRT use (Supplementary Table A.3).

Table 2
Relative Risk Ratios (RRR) and 95% Confidence Intervals (CI) for smoking status at follow-up by depressive symptoms at baseline (N = 1438).

Depressive symptoms predicting smoking status	Adjusted for age and sex			Adjusted for covariates[a]			Adjusted for covariates[a] and CPD		
	RRR	95% CI	*P*	RRR	95% CI	*P*	RRR	95% CI	*P*
Occasional smoker vs Daily smoker (ref)									
None/Minimal	1.00			1.00			1.00		
Mild	0.97	0.51–1.85	0.92	0.95	0.49–1.83	0.87	1.11	0.57–2.17	0.76
Moderate/Severe	0.55	0.17–1.82	0.33	0.62	0.18–2.09	0.44	0.86	0.25–2.98	0.82
Former smoker vs Daily smoker (ref)									
None/Minimal	1.00			1.00			1.00		
Mild	0.86	0.62–1.20	0.39	0.90	0.64–1.25	0.50	0.93	0.67–1.31	0.69
Moderate/severe	0.50	0.28–0.89	0.018	0.54	0.30–0.96	0.037	0.62	0.34–1.12	0.11

CPD = Cigarettes per day.
N = Total number.
[a] Age, sex, social class, health status, marital status, and heavy drinking occasions.

Table 3
Hazard Ratios (HR) and 95% Confidence Intervals (CI) for time to quitting (years) since baseline by depressive symptoms (N = 1280).

Depressive symptoms predicting quitting smoking	Adjusted for age and sex			Adjusted for covariates[a]			Adjusted for covariates[a] and CPD		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
None/Minimal	1.00			1.00			1.00		
Mild	0.83	0.62–1.11	0.22	0.87	0.64–1.16	0.34	0.89	0.66–1.19	0.42
Moderate/Severe	0.58	0.36–0.96	0.035	0.62	0.37–1.02	0.059	0.68	0.41–1.13	0.14

CPD = Cigarettes per day.
N = Total number.
[a] Age, sex, social class, health status, marital status, and heavy drinking occasions.

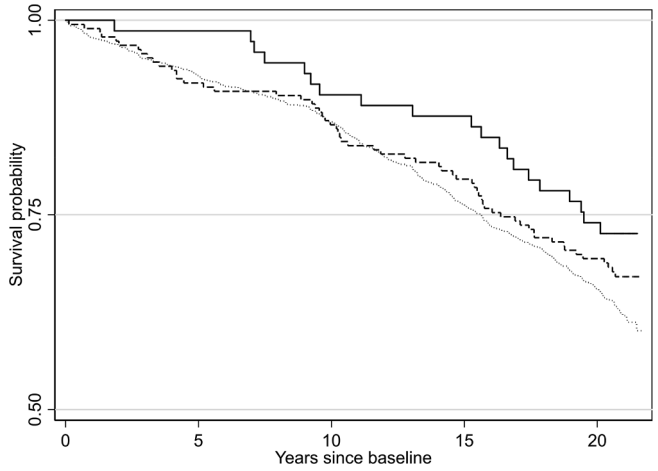

Fig. 1. Kaplan-Meier curves for quitting as a function of time (in years) since baseline by categories of depressive symptoms. The survival probability shows the fraction of baseline smokers who have quit by time since 1990. The dotted line (.....) is for smokers with none or minimal symptoms of depression, the dashed line (– – – –) for those with mild symptoms and the continuous line for those with moderate to severe symptoms.

4. Discussion

In a prospective 20-year follow-up study of daily smokers, we found higher level of depressive symptoms to predict lower likelihood of smoking cessation. The association appears to be robust when adjusting for multiple covariates, yet partly explained by smoking heaviness as well as by familial factors. Overall, our findings support and expand the earlier results that depressive symptoms predict less successful quitting (Hitsman et al., 2013; Huffman et al., 2018; Kenney et al., 2009).

We found that moderate/severe depressive symptoms predicted a lower likelihood of smoking cessation at follow-up. The time-to-event analysis further supported these findings. This is in line with a meta-analysis which found that depressed smokers had 17% lower odds of short-term abstinence and 19% lower odds of long-term abstinence compared to non-depressed (Hitsman et al., 2013). Furthermore, individuals with a history of two or more lifetime mental illnesses and comorbid depression were 66% less likely to quit smoking than those who had multiple mental illnesses but not depression (Huffman et al., 2018). Thus, overall, findings suggest depressive symptoms as a challenge for smoking cessation.

To control for the baseline differences in amount of smoking, CPD was added to the model, and the association attenuated modestly. This suggests that amount of smoking may have a role in the association between depression and smoking cessation. Apart from CPD, other substance abuse, such as alcohol abuse and dependence, may confound the relationship between depressive symptoms and smoking cessation (Kenney et al., 2009). However, in our sample heavy drinking did not influence the results. Further, although depressive symptoms seemed to associate with a lower likelihood to become an occasional smoker, the association was non-significant. In sensitivity analyses, the association between depression and quitting was not explained by differences in NRT use. However, a meta-analysis reported that NRT had a small, positive effect among depressed smokers (Gierisch, Bastian, Calhoun, McDuffie, and Williams, 2010).

Furthermore, the within-pair analysis found no association between depressive symptoms and smoking cessation, suggesting that the individual-level associations were, at least partially, due to shared familial influences. Consistent with our finding, an earlier twin study found a modest genetic correlation (r = 0.32) between depression and nicotine dependence (Edwards & Kendler, 2012), implying that persons having genetic vulnerability to depression also have a higher liability for nicotine dependence. In a recent genome-wide association meta-analysis, there was a modest genetic correlation (r = 0.26) between major depressive disorder and smoking cessation (Liu et al., 2019). In another twin study, the relationship among depression, regular tobacco use and nicotine dependence was explained partially by shared familial factors (Edwards, Maes, Pedersen, & Kendler, 2011). In contrast, a family study including first-degree relatives of the participants found no increased risk of smoking among relatives of the person with depression (Dierker, Avenevoli, Stolar, & Merikangas, 2002), not supporting a shared liability between depression and heavy smoking. Thus, understanding the role of shared familial factors for the relationship between depressive symptoms and smoking cessation remains a challenge for future studies.

There are several hypotheses why depressed smokers continue smoking and are less successful in quitting. The self-medication hypothesis states that individuals with a psychiatric condition smoke to relieve their symptoms (Khantzian, 2003). It is suggested that nicotine can lessen the symptoms of depression in the short-term and nicotine abstinence can accelerate withdrawal symptoms such as depressed mood (Bruijnzeel, 2012; Picciotto et al., 2002). Additionally, psychological mechanisms such as low positive affect, high negative affect, cognitive impairment, anhedonia, and anxiety sensitivity can hinder smoking cessation among depressed individuals (Ameringer & Leventhal, 2010; Leventhal & Zvolensky, 2015; Mathew et al., 2017). Other reasons include concern regarding weight gain, interaction with treatment for mental disorder (Royal College of Psychiatrists, 2013), ineffective cessation intervention, and failure in relapse prevention (Ruther et al., 2014). Moreover, it should be noted that low motivation to quit may be a symptom of depression itself, and lower self-efficacy may contribute to fewer quit attempts and/or seeking out treatments.

Effective smoking cessation interventions are needed for those suffering from depression. Pharmacological treatment and non-pharmacological approaches, for example, tailored quit line program, and an organizational change approach in behavioral health care settings are equally important (Secades-Villa et al., 2017; Steinberg, Weinberger, & Tidey, 2019). It is inevitable that depressed smokers require more support during smoking cessation, and combined interventions are necessary for addressing the disparity (Aldi, Bertoli, Ferraro, Pezzuto, & Cosci, 2018).

Our findings have implications for future research. We found that baseline amount of smoking and familial factors play a role in the association between depressive symptoms and smoking cessation. Most

smokers with psychiatric co-morbidities are interested in quitting but more research and development are required within smoking cessation treatments to understand which characteristics of the individual and the treatment are predictive of successful cessation, and how best to tailor the cessation programs for this vulnerable population group.

4.1. Strengths and limitations

Among the strengths of this study is that depressive symptoms were measured using BDI, a widely used and well-known instrument to capture self-rated depressive symptoms. Next, we were able to include a large sample of daily smokers at the baseline and assess changes in their smoking status for 20 years. This included not only quitters but also those who became non-daily smokers. Further, we were able to control for both measured covariates and unmeasured familial factors. The study findings among twins are generalizable to the general population because the information on twins was based on population-based sample with relatively high response rates, and twins are not different from singletons in terms of depression or smoking behavior (Kendler, Martin, Heath, & Eaves, 1995; Ware et al., 2016).

The extended follow-up period of 20-years is also a potential limitation as smoking status may have changed more than once, i.e. respondents may have quit smoking and relapsed again. Secondly, age at quitting was self-reported and retrospective in nature and can include recall bias; but it would be unlikely to depend on depression assessed at baseline. Third, we did not have information on baseline co-morbid psychiatric diagnoses. Fourth, the BDI mean score for the total sample was quite low: only 4.8% of participants scored 17 or more at the baseline. BDI score had a floor effect which is common in population-based samples. Underreporting is also a possibility in self-reported measures. Fifth, we used the baseline amount of smoking (CPD) to indicate smoking heaviness. It would have been optimal to also include Time to First Cigarette of the day as the other item of the Heaviness of Smoking Index, however, we only had information regarding CPD. Finally, in the within-twin pair analysis, the number of pairs was insufficient for conducting meaningful analyses separately by zygosity.

4.2. Conclusions

Our findings provide further support for a longitudinal association between depressive symptoms and lower likelihood of smoking cessation. This association may partly be explained by the baseline amount of smoking and shared familial factors. To deepen understanding on the role of depression in smoking cessation, it is crucial to examine the underlying mechanisms that may explain this association. Smoking cessation interventions and treatments should monitor depressive symptoms throughout both before and after the quitting.

CRediT authorship contribution statement

Anu Ranjit: Conceptualization, Data curation, Methodology, Software, Formal analysis, Writing - original draft, Writing - review & editing, Visualization. **Antti Latvala:** Conceptualization, Funding acquisition, Methodology, Software, Supervision, Validation, Writing - review & editing. **Taru H Kinnunen:** Writing - review & editing. **Jaakko Kaprio:** Conceptualization, Data curation, Funding acquisition, Project administration, Resources, Writing - review & editing. **Tellervo Korhonen:** Conceptualization, Funding acquisition, Supervision, Validation, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2020.106427.

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